Bony orbital development after early enucleation in humans

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Abstract

**Aim**—To analyse the extent of bony orbital volume reduction after enucleation in humans.

**Methods**—Volumetric studies on bony orbital volumes based on three dimensional reconstructions acquired from high resolution computed tomograph (CT) scans were performed in 29 patients with acquired anophthalmia and four patients before enucleation (controls). Eight patients (follow up 25–52 years) were enucleated in childhood aged between 0.4 and 8 years (group I), 21 in adulthood aged between 15 and 53 years. Fifteen of these patients (group IIa) had long standing anophthalmia (follow up 7–53 years), six patients (group IIb) were enucleated 9 months to 4 years before CT.

**Results**—Bony orbital volumes were reduced in all patients with long standing anophthalmia. The median percentage reduction in enucleated orbits was 7.0% in group I, 3.8% in group IIa, and 1.9% in group IIb. In patients with long standing anophthalmia (I and IIa) the reductions were statistically significantly different (p <0.01) from zero. There was some evidence of a correlation between orbital volume reduction and age at enucleation (rho = 0.36, p = 0.09, Spearman rank correlation coefficient) and a statistically significant correlation between volume reduction and time interval since enucleation (rho = −0.5, p = 0.003). Clinically none of the patients showed significant facial asymmetry.

**Conclusions**—These data provide strong evidence that enucleation both in children and adults is associated with a reduction of bony orbital volume and that this decrease in volume is associated with increasing time. However, the reduction is smaller than generally assumed and does not cause obvious facial asymmetry. It is more related to the time interval since enucleation than the age at enucleation, which makes a mechanism of volume adaptation more likely than just retardation of growth.

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Orbital growth is believed to be checked following enucleation in childhood, resulting in malformation and facial asymmetry depending upon the age at which enucleation was performed.¹² This was already suspected in the 19th century, when the first experiments on animals were performed.¹³¹⁴ Based on animal research, Kennedy⁵ and Sarnat⁶–⁸ supported and finally established the theory of the detrimental influence of early enucleation on orbital growth. This belief, however, rarely corresponds to our clinical observations in humans and the appearance of anophthalmic patients enucleated in childhood. The interesting question as to what extent bony orbital growth is affected by early enucleation in humans remains unanswered. We attempt to address this question.

**Patients and methods**

Twenty nine patients (14 female, 15 male) with acquired anophthalmia were examined clinically and with high resolution computed tomography (CT). Patients with conditions possibly causing facial asymmetry, such as orbital fractures, phthisical eye, congenital or...
Table 1 Absolute and relative bony orbital volumes (BOV) after enucleation

<table>
<thead>
<tr>
<th>Patients</th>
<th>No</th>
<th>Age at enucleation (years)</th>
<th>Time between enucleation and CT (years)</th>
<th>BOV difference enucleation − norm (ml)</th>
<th>Relative BOV difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>8</td>
<td>Median (range) 3.3 (0.4–8)</td>
<td>Median (range) 30.5 (25–52)</td>
<td>−1.7 (−3.0, −1.5)</td>
<td>−7.0% (−9.9%, −5.4%)*</td>
</tr>
<tr>
<td>IIa</td>
<td>15</td>
<td>Median (range) 23 (13–52)</td>
<td>Median (range) 12 (7–53)</td>
<td>−0.9 (−2.1, −0.4)</td>
<td>−3.8% (−7.9%, −1.7%)</td>
</tr>
<tr>
<td>IIb</td>
<td>6</td>
<td>Median (range) 41 (25–53)</td>
<td>Median (range) 1.4 (0.8–4)</td>
<td>−0.4 (−1.4, −0.01)</td>
<td>−1.9% (−5.0%, 0%)</td>
</tr>
<tr>
<td>Controls</td>
<td>4</td>
<td>Median (range) 3.4 (0.6–8)</td>
<td>Median (range) 1.1 (0–4)</td>
<td>−0.19 (−0.38, 0.05)</td>
<td>−0.8% (−1.3%, 0.15%)</td>
</tr>
</tbody>
</table>

*p < 0.01, IQ = interquartile.
There was also a mild, but insignificant, decrease of the BOV in group IIb of −0.4 ml (−1.3, −0.01 ml), corresponding to −1.9% relative difference (−5.03%, 0%). The greatest reduction seen in the four controls was −1.8 ml (Table 1).

The relative orbital volume differences for each patient and controls are shown in Figure 3. There were no differences in BOV reduction between patients with and without primary orbital implants.

Median values of all groups are illustrated in Figure 4. The relation between age at enucleation and BOV is shown in a scatter diagram (Fig 5) for patients in groups I and IIa. We found some evidence (not statistically significant) of a positive correlation between the age at enucleation and the BOV difference (rho = 0.36, p = 0.09).

There was evidence, however, of a correlation between the influence of the time interval since enucleation and the BOV difference (rho = −0.56, p = 0.003) (Fig 6).

Clinically none of the patients showed signs of facial asymmetry. This is even true for the patient with the largest relative volume difference of −14.7% (Fig 7).

Discussion

“Among the apparent truisms in ophthalmology, there is one, at least, which requires close scrutiny. This is the belief that orbital growth is checked following enucleation in childhood, resulting in more or less maldevelopment and facial asymmetry depending upon the age at which enucleation was performed.” With these sentences Howard begins his article on orbital growth after unilateral enucleation in childhood.10

However, in a series of 15 patients enucleated under the age of 12 years he did not find a significant decrease of the orbital size or asymmetry. He concluded that enucleation of one eye in infancy or childhood is associated with a small reduction in the size of the bony orbit in later years, but that this reduction is not of cosmetic consequence. The same opinion had been expressed by Gordon Byers from Moorfields Eye Hospital in 1898, based on his study on 10 patients enucleated during childhood.11 Following his report he detected no arrest of development. His observations were questioned by others.12 13 Thomson12 carried out experimental enucleations in young rabbits. His results have been considered to show conclusively that, in rabbits, a deficiency of growth occurs in the anophthalmic orbit. In the 1960s Kennedy5 and Sarnat6 began their extensive studies on the effect of early enucleation on the orbit. They found significant reductions of the orbital size particularly in the animal model. Based on approximate estimations, Kennedy5 calculated the decrease in the orbital volume up to 19.5% in patients with orbital implants and up to 27.7% in patients without orbital implants. He assumed that the volume reduction after enucleation can reach...
the magnitude of 35–50%. Their work was of fundamental importance to the understanding of the problem of early enucleation and persistently influenced the point of view of ophthalmologists. Up to now it has been generally accepted that early enucleation causes harmful maldevelopment of the enucleated orbit.14–20

Can our results on three dimensional reconstructions and orbital volumetry in anophthalmic patients add any new aspects to this thoroughly discussed issue? Yes, because for the first time exact volumetric data on a larger series of anophthalmic humans in vivo with very long follow ups are available. Our volumetric studies based on high resolution CT scans confirm a reduction of the anophthalmic bony orbit in patients enucleated in their early childhood. However, the volume reduction is smaller than generally assumed. In our patients we found that the greatest reduction of the anophthalmic orbit compared with the fellow orbit was 14.5% which is less than the few volumetric data given in the literature, where volume reductions were calculated at between 19.5% and 50%.2 5

Interestingly, we also found a statistically significant reduction of the BOV in patients who were enucleated when they were grown up. In this adult group the volume deficit reached up to 4 ml and the median reduction almost −4% in the enucleated orbit 12 years after enucleation. The adult bony orbit has been regarded as a stable compartment not being influenced by enucleation.18–22 This is obviously not the case. However, there are some early observations suggesting that enucleation might induce shrinkage of the bony orbit20–27 which had not yet been proved.

Correlation analysis of BOV changes versus age at enucleation and time interval since enucleation shows a stronger association between reduction of BOV and the time course than age at surgery.

There was no difference between patients with and without primary orbital implants, suggesting that the post-enucleation bony orbital development in humans may not be influenced by implants. Small numbers (4/4) make statistical analysis not applicable. However, in none of our patients was clinically obvious facial asymmetry noticed. This is consistent with reports in the literature on patients who had been enucleated during childhood and who showed no significant facial malformation despite differences in radiological features.20 22 Recently Fountian et al examined nine patients 5–10 years after enucleation during early childhood (age 0.4–6 years). Morphometric measurements of five linear orbital dimensions using a millimetre rule were collected. They found no statistically significant difference in any of the measured orbital dimensions between the enucleated and fellow orbits, which was attributed to the presence of an orbital implant.28 However, their observation, which is consistent with our clinical impression, is more understandable because of the small volume reductions, which cannot be detected by our methods. Rough linear measurements than the fact, that all nine patients had primary orbital implants. In our series at least there is no evidence that orbital implants influence BOV after early enucleation.

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